



Treatment of ectopic pregnancy with methotrexate

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Dear Sirs,

The recently published retrospective study of Brunello et al. investigates the impact of β hCG and progesterone level on methotrexate (MTX) treatment success, in patients with tubal ectopic pregnancy [1].

Despite the well-designed study protocol and the promising results, investigating the β hCG's value as a prognostic factor for MTX treatment outcome, MTX safety needs to be elucidated. Moreover, except from mentioning that MTX has “high success rate and tolerance” together with the “repeated measures of MTX” used in this study, the official off-label character of its administration in the ectopic pregnancy should be underlined.

MTX's main indications include neoplastic diseases, psoriasis and rheumatoid arthritis [2], while despite its extensive use in the clinical practice, there is no indication for use in the treatment of ectopic pregnancy according to the European Medicinal Agency (EMA) [3].

Additionally, in European countries, there is a special concern about MTX use as the European Medicinal Agency is until now conducting a review about MTX administration and safety initiated at the request of Spain, under Article 31 of Directive 2001/83/EC [3]. Moreover, 3 years ago, the French College of Gynecology and Obstetrics (CNGOF) published an overview about the off-label use of MTX in ectopic pregnancy stating that it is a temporary recommended drug [4].

There are several case reports indicating severe toxicity and mortality following MTX administration in ectopic pregnancies. The former side effects have occurred in either single, double or multi-dosage scheme in women with no pre-existing health problems. Specifically, a 26-year-old

woman was treated with a 78 mg intramuscular injection of MTX and soon after the administration presented symptoms of bilateral paresthesia of the lower limbs, and finally was diagnosed with transverse myelitis [5]. Two more similar life-threatening situations were also described, when two patients presented with neutropenia and febrile morbidity after administration of MTX for ectopic pregnancy, one in single dose and the other after receiving three doses [6]. Many more case reports describe life threatening or even fatal conditions due to this off-label use.

The value of MTX administration in women with ectopic pregnancy is undeniable. However, its off-label use, especially in repeated doses, should be well noted, while raising awareness could help advocating the drug's safety.

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Compliance with ethical standards

Conflict of interest All authors declare that have no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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